

Example 10

siRNA constructs prepared and tested against eIF4E and Survivin targets

Selected siRNA constructs were prepared and tested for their ability to lower targeted RNA as measured by RT-PCR. The IC₅₀ of each construct was determined.

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SEQ ID No: ISIS No: Constructs targeted to eIF4E (5'-3'):

Mixed 2'-F/2'-OCH₃ as/s RNA

25 (as) eIF4E	349890	UfGfUfcAfUmAmUfUfCmCmUfGfGfAfUfCfCmUmUm
26 (s) eIF4E	338935	AAGGAUCCAGGAAUAGACA
27 (as) eIF4E	349891	UfCfCfUfGfGmAmUfCfCmUmUfCfAfCfCfAfAmUmGm
28 (s) eIF4E	338939	CAUUGGUGAAGGAUCCAGGA
29(as) eIF4E	349892	UfCfUfUfAfUmCmAfCfCmUmUfUfAfGfCfUfCmUmAm
30 (s) eIF4E	338943	UAGAGCUAAAGGUGAUAAA
31 (as) eIF4E	351097	AfUfAfCfUfCmAmGfAfAmGmGfUfGfUfCfUfUmCmUm
15 32 (s) eIF4E	338952	AGAACAGCACCUUCUGAGUAU
		Full P=S RNA as/s full 2'-OCH₃
35 (as) Survivin	346280	UrsUrsUrsGrsArsArsArsUrsGrsUrsUrsGrsArsUrsCrsUrsCrsU
34 (s) Survivin	352512	GmGmAmGmAmUmCmAmAmCmAmUmUmUmUmCmAmAmAm
		Full P=S RNA as/s full 2'-OCH₃ except terminal nucleosides
20 35 (as) Survivin	346280	UrsUrsUrsGrsArsArsArsUrsGrsUrsUrsGrsArsUrsCrsUrsCrsCrsU
34 (s) Survivin	352513	GGmAmGmAmUmCmAmAmCmAmUmUmUmUmCmAmAmAm

SEQ ID No: ISIS No: Constructs targeted to Survivin (5'-3'):

Mixed 2'-F/2'-OCH₃ as/s RNA

25	33 (as) Survivin	355711	UfUfUfGfAfAmAmUfUfGmUmUfGfAfUfCfUmCmCm
	34 (s) Survivin	343868	GGAGAUCAACAUUUCAA

Lowercase f indicates that the preceding nucleoside is a 2'-F nucleoside (Cf = 2'-F cytidine). Lowercase m indicates the previous nucleoside is a 2'-OCH₃ nucleoside.

30 Lowercase s (second lowercase letter following a U, A, G, or C) after a lowercase letter indicates that the internucleoside linkage is a phosphorothioate internucleoside linkage (rs = the sugar is ribose and the internucleoside linkage is phosphorothioate).

The above constructs were tested in HeLa cells, MH-S cells or U-87 MG cells using a standard assay as shown in Example 15. The IC₅₀'s were calculated as shown 35 below.